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EXPERIMENTAL STUDIES ON THE BEHAVIOR OF THE GALLBLADDER AFTER CHOLEDOCHOJEJUNOSTOMY

by

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CHAPTER I. INTRODUCTION

Excision of the head of the pancreas and of the duodenum or total excision of the pancreas and duodenum is nowadays recommended as a radical treatment of a tumor of Vater's papilla and of cancer of the pancreas. In either case choledochojejunostomy is required. This anastomosis is also performed in the treatment of stenosis or occlusion of the common bile duct, and quite recently, of chronic relapsing pancreatitis.

The outflow of bile goes on without obstruction as long as the complicated intra-and extrahepatic biliary systems keep it under proper control, but the flow is obstructed if the systems fail to regulate it properly for some reason or other. It is therefore conceivable that choledochojejunostomy, which deprives the system of the sphincter of Oddi without providing its substitute in any form, may produce some change in the outflow of bile. Does the operation leave the functions of the gallbladder undisturbed? Does it cause the functional extinction and atrophy of the organ after a period of time? Or does it turn the organ into a sort of diverticulum and an obnoxious relic causative of inflammation?

If the gallbladder retains its functions after choledochojejunostomy, it deserves to be left intact. If it loses its functions, it may be excised at the time of the anastomosis. If the presence of the gallbladder after it proves harmful, the organ should be removed.

According to ANDO, the gallbladder becomes atrophied in cats in which the sphincter of Oddi has been kept functionless for a month or so by a small glass tube inserted and fixed in the terminal part of the common bile duct. He infers from this fact that atrophy of the gallbladder may be brought about when the common bile duct is left open at its termination.

LARGE found that histological study of the gallbladder, biliary duct and the liver in dogs sujected to choledochoduodenostomy reveals a marked ascending infection of the biliary duct.

The present author examined in dogs submitted to choledochojejunostomy the functions of the gallbladder and the macroscopical and histological pictures of the liver, biliary duct and the gallbladder, with a view to settling the problem whether the gallbladder should be excised or left intact when the common bile duct is to be anastomosed to the jejunum.

CHAPTER II. EXPERIMENTAL CHOLEDOCHOJEJUNOSTOMY

1. Animals and Method

i. Animals used: Adult dogs weighing about 10 kg.

ii. Method: As illustrated in Fig 1, Roux-Y shaped anastomosis. The intestine was cut at a point in the upper part of the jejunum for choledochojejunostomy and enteroentero anastomosis. The two sites of anastomosis were kept approximately 30 cm apart, and penicillin, 0.6 to 1 million u., was used during and after the operation, in order to prevent any possible ascending infection reaching the gallbladder.

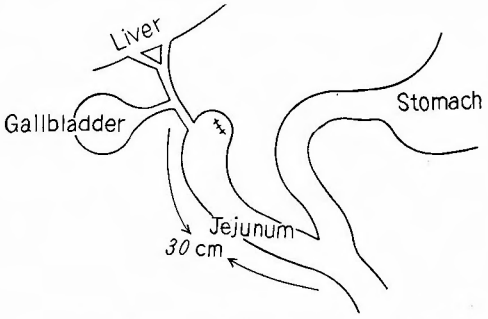


Fig. 1 Roux-Yshaped anastomosis

The common bile duct is so small and thin-walled in dogs that choledochojejunostomy is extremely difficult to perform. A new and simple method which would facilitate the operation and prevent any postoperative stenosis and occlusion had to be worked out. The method adopted after comparative evaluation of the merits of many similar methods is as follows:

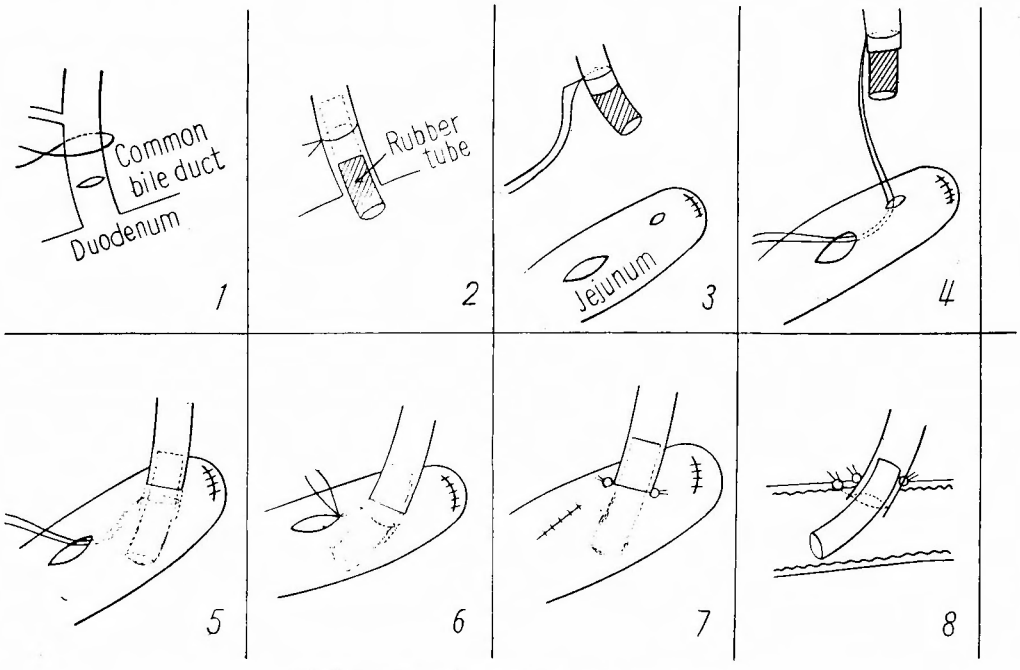


Fig. 2 Method of choledochojejunostomy

As illustrated in Fig 2, after the common bile duct is cut, a rubber tube is inserted into its hepatic side and fixed there with a silk thread. The free end of the thread is passed into the intestinal canal through the jejunal wall previously

incized and drawn out through the other part of the wall. The thread is then drawn tight, and the cut end of the common bile duct is brought close to the first part of the intestine. Choledochojejunostomy is now completed. The second incized part of the intestine is then closed up and the anastomosed part is so treated as to be covered over by the large omentum.

2. Postoperative Variation in the Level of Total Serum Bilirubin

Changes that may be followed after choledochojejunostomy in the amount of bile passing through the common bile duct were examined daily by electrophotometric determination of the value of total serum bilirubin after the method of Evelyn-Malloy. As illustrated in Fig 3, a slight rise in the value of total serum bilirubin occurred between 3rd and 10th postoperative day, but the value soon returned to normal. This temporary elevation, in all probability, signified temporary obstruction of passage due to edma in the anastomosed area. Dogs in which this rise in the value of total serum bilirubin continued for a long time or occurred at later date were excluded from this experiment.

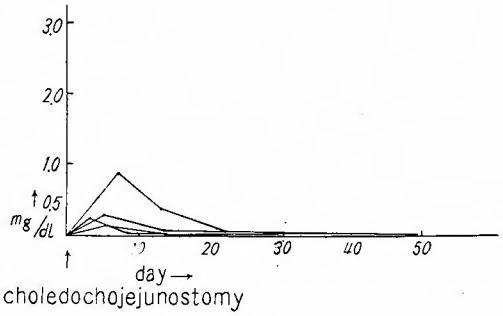


Fig. 3 Variation in the level of total serum bilirubin after choledochojejunostomy

CHAPTER III. BILE-CONCENTRATING FUNCTION OF THE GALLBLADDER

As demonstrated first by Brand and confirmed later by other workers, the gallbladder performs bile-concentrating function. According to Raus & McMaster, the gallbladder of the dog is capable of raising the concentration of bile 7. 1 times within 24 hours.

Mann & Bollman demonstrated in dogs that ligation of the common bile duct is not followed in 24 to 36 hours by any variation in the value of serum bilirubin but that ligation simultaneously accompanied by excision of the gallbladder causes a rise in the value within 24 hours after operation. This finding proves that the gallbladder has a bile-concentrating function and that this function is not unlimited in its power. The present author, by applying Mann & Bollman's experiment, examined this function of the gallbladder in dogs subjected to choledochojejunostomy.

1. Method

The level of total serum bilirubin was determined daily in dogs in which choledochojejunostomy and, after a definite interval, ligation of the common bile duct has been performed, and for comparison, in normal dogs in which only ligation of the common bile duct has been conducted, and in other normal dogs in which the gallbladder has been removed at the time of ligation of the common bile duct.

(1) Preoperative treatment:

The dogs were kept fasting on the day of operation.

(2) Anesthetic used:

Sodium Isomytal, 0.03 to 0.05 g per kilogram of body weight, given intravenously.

(3) Method of ligation of the common bile duct:

After laparotomy the duct was doubly ligated and cut its terminal portion under the intraabdominal administration of penicillin, 200,000 u. Postoperatively the dogs were given no food except water, and the level of total serum bilirubin was determined early each morning when the stomach was empty.

2. Results: Variation in the level of total serum bilirubin in the three groups of dogs

A. In normal dogs with the common bile duct ligated: (Table 1)

The level remained within its normal range in all cases on the lst day after ligation, rose above normal in some cases on the 2nd after ligation, was above normal in all cases on the 3rd after ligation, and continued to rise in all cases as time progressed, reaching its peak between the 7th and 10th after ligation. The peak varied considerably from case to case.

B. In normal dogs with the gallbladder removed and the common bile duct ligated: (Table 2)

Ligation was soon followed by a remarkable rise. A rise above normal was noted in some cases as early as 7 hours after ligation. The value rose to 1 mg/dl or more in all cases within 24 hours, and to its peak between the 2nd and the 4th after ligation.

C. In dogs in which choledochojejunostomy was later followed by ligation of the common bile duct: (Table 3)

Six dogs in which ligation of the common bile duct was made on the 28th day (dog A), 31st (dog B), 34th (dog C), 40th (dog D), 64th (dog E), and 75th day (dog F) after choledochojejunostomy, were examined for estimation of total serum bilirubin value. In dogs A and B the level of total serum bilirubin was within its normal range on the lst day after ligation, was slightly above normal on the 2nd after ligation, and thereafter continued to rise gradually until it reached its peak on or about the 6th after ligation. In dogs C and D it rose to 1 mg/dl or more already on the lst day after ligation … a level reached in dogs in which choledochojejunostomy and removal of the gallbladder were performed at the same time … and reached its peak on or about the 4th after ligation. In dogs E and F

Table 1 Total serum bilirubin the normal dogs with the common bile duct ligated. (mg/dl)

Dog. No.	Preop	Postop day 1	2	3	4	5	6	7	8	9
2	0.15	0.2	0.56	0.56	0.75	1.8	3.21	3.68	4.0	
9	0.19	0.14	0.19	0.36	0.36		0.55	1.2	2.0	2.8
11	0.14	0.18	0.25	0.23	0.3	0.38	0.38	0.65	1.56	1.56
16	0.11	0.14	0.24	1.4	3.25	5.2	5.2		4.0	
18	0.15	0.28	0.52	1.22	0.94	1.78	2.08	2.5	2.7	3.4
21	0.13	0.15	0.47	0.83		1.4	1.3	1.3	1.8	1.95
22	0	0.15	0.3	0.83	1.1	1.75	2.55	4.3	5.9	5.0

Table 2 Total serum bilirubin in the normal dogs with the gallbladder removed and the common bile duct ligated. (mg/dl)

Dog. No.	Preop	Postop day 1	2	3	4	5	6	7	8
6	0.2	1.12	1.82	4.14	5.9	5.75	5.13	6.63	
10	0.14	2.44	5.06	5.45	5.34	4.58	4.0		6.0
13	0.23	1.3	2.67	3.5	6.0	5.62	6.15	5.5	

Table 3 Total serum bilirubin in the dogs in which choledochojejunostomy was later followed by ligation of the common bile duct. (mg/dl)

Dog. No.	Preop	Postop day 1	2	3	4	5	6	7
14 (A)	0.09	0.19	0.93	2.05	2.6	4.0	6.95	5.97
24 (B)	0.14	2.5						
25 (C)	0.09	0.19	1.02	2.00	2.95	4.2	4.45	4.1
27 (D)	0.18	1.8	2.9	3.7	6.3	5.95	5.0	4.3
37 (E)	0	0.64	2.08	3.0	5.1	4.05	4.55	5.75
62 (F)	0	0.85	1.55	3.25	4.05	3.5	3.4	3.5

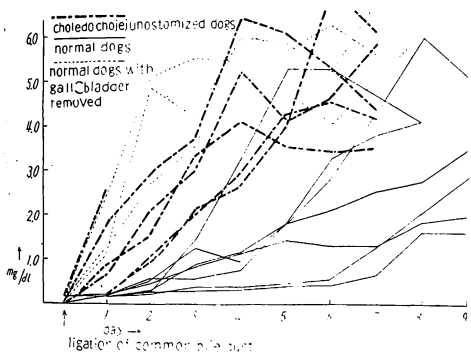


Fig. 4 Variation in the level of the total serum bilirubin in the three groups of dogs with common bile duct ligated.

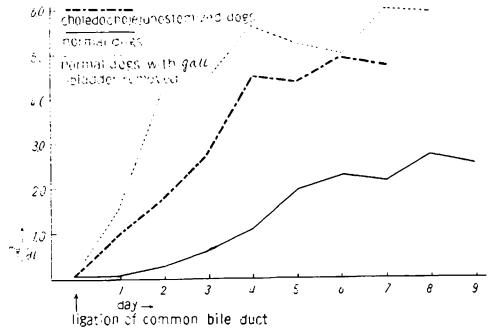


Fig. 5 Variation in the average level of the total serum bilirubin in the three groups of dogs with common bile duct ligated

it rose at a slower rate than in dogs C and D, but was already above normal on the 1st day after ligation, reaching its peak on or about 4th after ligation. (Fig. 4)

As illustrated in Fig. 5, the level of total serum bilirubin in those six dogs, when averaged and shown in a curve, stands between that in the normal dogs with the common bile duct ligated and that in the normal dogs with the common bile duct ligated and the gallbladder excised simultaneously.

Supplementary Experiment

The bile secretion after choledochojejunostomy was determined as follows:

1. Procedure

Laparotomy was performed under general ether anesthesia; the common bile

duct ligated; a vinyl tube inserted into the common bile duct and fixed there; after the animals regained consciousness, the amount of bile sent out of the body through this tube was measured hourly for 5 hours.

2. Results

As illustrated in Fig. 6, the hourly measurements showed that in normal dogs the amount of bile secreted per hour ranged from 0.6 to 3.44 cc, and that the hourly secretion was 1.3 to 3.7 cc in dogs in which choledochojejunostomy was performed. Thus there was no marked difference between the two groups. Autopsy showed that this anastomosis was not followed by occlusion of the cystic duct in any of the dogs so treated.

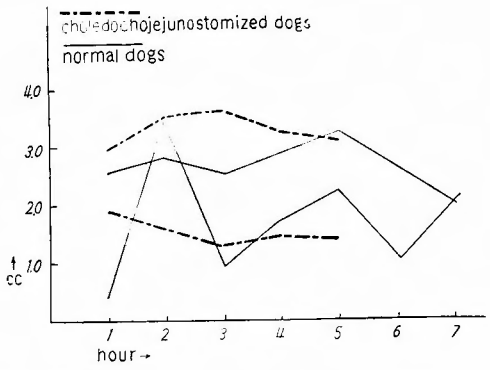


Fig. 6 Variation in the quantity of bile secretion of the choledochojejunostomized dogs and the normal dogs

CHAPTER IV. MOTILE FUNCTION OF THE GALLBLADDER

The motility of the gallbladder was first noted by Doyon et al. and has since been studied and confirmed by other workers; X-ray examination and macroscopical observation on laparotomy of the organ, tracing of its internal pressure performed on living body of an extirpated gallbladder, and above all, the discovery by Graham & Cole of cholecystography with a contrast medium, have combined to promote the study.

According to the authors above-named, the movement of the gallbladder consists of tardy tonic contractions and rhythmical proper movement ··· tonic contractions and tonus rhythm in Ivy's classification.

The nervous control of the gallbladder remains unexplained for its complexity. A majority of workers agree that the movement of the organ may be accelerated by the parasympathetic and inhibited by the sympathetic.

Lieb and Whoter saw that the gallbladder contracts when acted upon by pilocarpine; Bronner, that egg-yolk acts on the gallbladder most effectively by making it contract and expell nearly all of the bile contained in it ··· a fact confirmed by many other workers by cholecystography; and Ivy, that cholecystochinin, a name he gave to the active principle extracted from the mucosa of the duodenumn after egg-yolk is infused into it, causes in dogs and humans the flow of bile into the duodenum and increases the internal pressure of the gallbladder when it is given intravenously.

1. Method

The dogs were kept fasting on the day of experiment, 20 to 30 minutes after subcutaneous administration of 1% morphine hydrochloride 3.0 to 4.0 cc general anesthesia by ether was inducted.

The dogs were fixed in dorsal position on the operating table, a median incision was made in the upper abdominal region for exposure of the gallbladder; the gallbladder was punctured at its base and about two-thirds of the bile was aspirated out; a small incision was made across the punctured part of the gallbladder wall and through it a rubber balloon with a rubber tube attached to it was inserted into the gallbladder. The opening left in the gallbladder wall was so closed up by suture as to leave the rubber tube unobstructed. The free end of the rubber tube was connected to a tambour and to a water manometer, and some 7 cc of air was sent in to inflate the balloon and increase the manometric pressure to 70 to 100 mm; the movement of the gallbladder was now easily traceable. On the other hand, a small incision was made through the anterior wall of the stomach near its pyloric region, and through this small opening a rubber tube was inserted till its foremost part was introduced into the duodenum.

Subsequent to this procedure, the lower half of the incision in the abdominal wall was closed but the lower half was left open lest the intestine be pushed out because of the abdominal pressure after the animals regained consciousness ··· a measure designed to minimize any possible effect of the abdominal pressure.

On the dogs thus prepared the following experiments were made when the dogs had fully awakened from anesthesia.

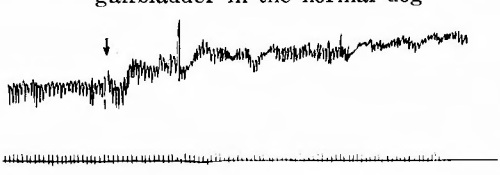
As a means of inducing tonic contraction of the gallbladder, some 20 cc of a creamy mixture of butter and egg-yolk was sent into duodenumn through the rubber tube connecting the stomach to the duodenum, and next, after a definite period of time, 0.4 to 0.5 cc of 1% pilocarpine hydrochloride was administered subcutaneously.

2. Results

Preliminary Experiment I.

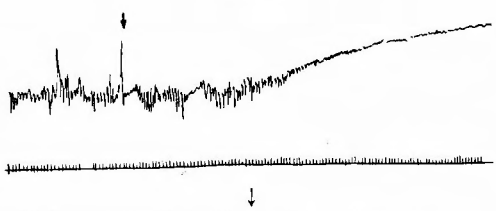
The gallbladder was found to contract in normal dogs which had received the creamy mixture into the duodenum or 1% pilocarpine hydrochlolide by subcutaneous injection, the latter substance inducing more marked contractions than the former. (Fig. 7, Fig. 8)

Fig. 7 Variation of the internal pressure of gallbladder in the normal dog



Infusion of the creamy mixture into duodenum (Time 5sec)

Fig. 8



Subctaneous injection of 1% Pilocarpine hydrochloride (Time 5sec)

In this experiment, however, it would be impossible to ascertain whether gallbladder contractions in dogs subjected to choledochojejunostomy could be induced or not, for in such dogs the common bile duct is open at its termination into the jejunum. In order to clarify this problem, other preliminary experiments were

carried out.

Preliminary Experiment II.

The common bile duct was completely cut transversely, and a small opening was made on the duodenum, and then the cut end of the hepatic side of the former was connected to the opening of the latter by means of a rubber tube. The same apparatus as in the preceding experiments was used here. The results revealed that neither the creamy mixture injected into the duodenum nor the 1% pilocarpine hydrochloride given subcutaneously caused any contraction of the gallbladder after choledochojejunostomy. The reason for this is considered to be that because the common bile duct was left open at its distal end into the intestinal canal the flow of bile through the biliary duct was disturbed and the gallbladder did not receive a sufficient amount of bile to be filled up with it and that the bile in the gallbladder was easily sent into the duodenum when the air sent into the rubber balloon increased the internal pressure of the gallbladder.

Preliminary Experiment III.

As illustrated in Fig. 9 the common bile duct was cut transversely and its cut end of the hepatic side was fixed in position with a vinyl tube inserted into it; the free end of the tube was left out of the body. a rubber ballon was next

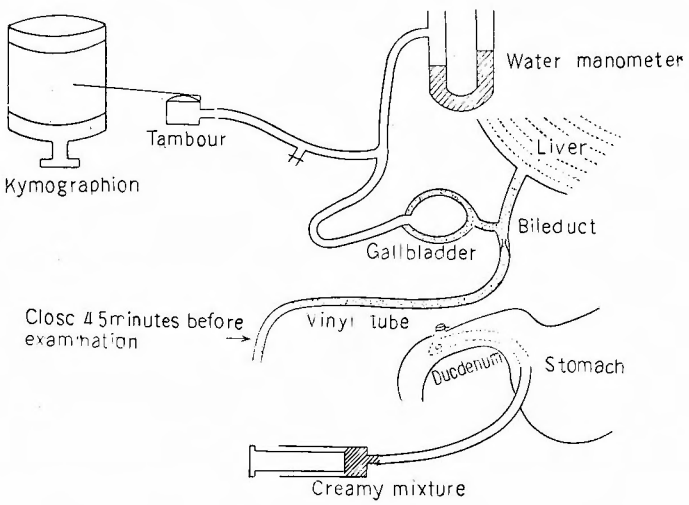
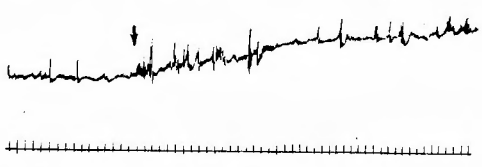


Fig. 9 Apparatus for measuring the internal pressure of the gallbladder

Fig. 10 Variation of the internal pressure of gallbladder in the normal dog



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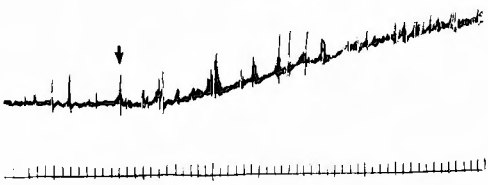
Infusion of the creamy mixture into duodenum (Time 15sec)

Fig. 11



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Subctaneous injection of 1% Pilocarpine hydrochloride (Time 15sec)

inserted into the gallbladder. The free end of the vinyl tube was closed at 45 minutes before examination so that the bile would accumulate in the biliary duct and the gallbladder in the meantime. The examination of the gallbladder, with water manometer pressure at 70 to 100 mm, showed that the creamy mixture infused into the duodenum or the 1% pilocarpine hydrochloride given subcutaneously induced contraction of the gallbladder. This procedure, therefore, was adopted for the final experiment in which the motility of the gallbladder was to be examined. (Fig. 10, Fig. 11)

Final Experiment

To examine motility or nonmotility of the gallbladder in dogs subjected to choledochojejunostomy, the method and apparatus for Preliminary Experiment III were used on the 30th, 65th and 98th day after choledochojejunostomy. It was found that infusion of the creamy mixture of butter and egg-yolk into the duodenum failed to induce contraction of the gallbladder in all three cases, but that subcutaneous injection of 1% pilocarpine hydrochloride caused contraction of the organ in two of the cases (65th day and 98th day), the third having been exempted from the examination for certain reasons. (Fig. 12, Fig. 13, Fig. 14, Fig. 15)

Fig. 12 Variation of the internal pressure of gallbladder in the dog on 65th day after choledochojejunostomy

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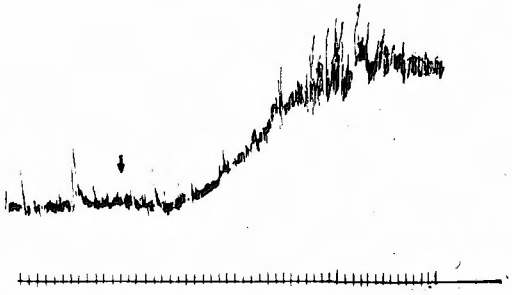
Infusion of the creamy mixture into duodenum (Time 15sec)

Fig. 13



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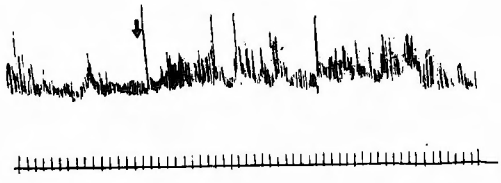
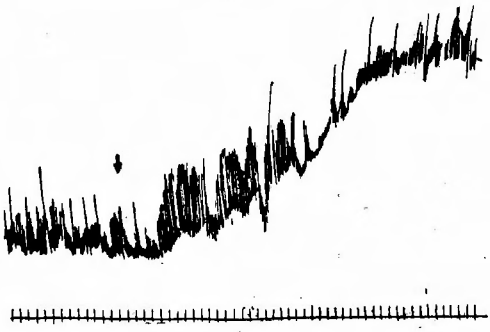
Subcutaneous injection of 1% Pilocarpine hydrochloride (Time 15sec)

Fig. 14 Variation of the internal pressure of gallbladder in the dog on 98 th day after choledochojejunostomy



Infusion of the creamy mixture into duodenum (Time 15sec)

Fig. 15



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Subcutaneous injection of 1% Pilocarpine hydrochloride (Time 15sec)

CHAPTER V. THE CAPACITY OF THE GALLBLADDER AS BILE RESERVOIR

In addition to the bile-concentrating function and motility that have been studied in the preceding experiments, the gallbladder must fulfill a third function, namely bile-storing, if it is to work properly as an efficient organ. These three functions are coordinated closely. The organ would lose much of its physiological significance without any of the functions. It is therefore an interesting feature of this series of experiments to find out whether or not the gallbladder is capable of storing bile in it when the common bile duct is left open at its terminal end after choledochojejunostomy. Cholecystography was conducted in dogs subjected previously to this anastomosis. This examination was undertaken on the theory that while negative results in such dogs could not be conclusive proof for any judgement regarding the bile-storing function positive results could provide basis for inferring presence of the bile storing function.

1. Method

Injection into the femoral vein of 20% biligrafin in a dose of 1.5 cc per kilogram of body weight was followed at half an hour, one, two, three, four and five hours by roentogenographic examination of the gallbladder.

2. Results

In normal dogs: As illustrated in Fig. 16 an ill-defined shadow was seen one hour after the injection, a highly well-defined shadow two hours, and an equally well-defined shadow three, four and five hours after the injection.

In three dogs subjected to choledochojejunostomy: Examination was made in those dogs on the 59th, 91st, and 164th postoberative day respectively. In the dog examined on the 164th day as illustrated in Fig. 17, the injection was followed at two hours by the appearance of the gallbladder as an ill-defined shadow which, unlike in the normal dogs, did not grow any clearer as time progressed. In the other two dogs (examined on the 59th and the 91st day) no shadow appeared at any time after injection.

CHAPTER VI. MACROSCOPIC AND HISTOLOGICAL PICTURES OF THE GALLBLADDER, THE BILIARY DUCTS, AND THE LIVER IN DOGS SUBJECTED TO CHOLEDOCHOJEJUNOSTOMY

1. Macroscopic Pictures (Table 4)

(1) The extrahepatic biliary ducts were thickened and dilated in all cases.

(2) The gallbladder was about normal-sized in some cases and slightly enlarged in others, showing no signs of atrophy in any case.

(3) The gallbladder wall was thickened and loosely adhered to the surrounding tissues in all cases, but there were no signs of acute cholecystitis in any case.

(4) The liver remained about normal except in one case in which abscesses were found.

(5) The formation of sandlike gallstones was found in 10 of 18 cases (an incidence of approximately 56%). Food residuals (broken pieces of straw) were found mingled with those tiny gallstones. (Fig. 18) In all cases the bile was turbid, and foul-smelling. In extreme cases it was muddy and extremely foul-

smelling. Its color was dark brown or yellow, and not dark-greenish-brown as in a normal gallbladder.

Table 4 Macroscopic pictures of the gallbladder, the liver, the extrahepatic bile duct, and the bile of the choledochojejunostomized dogs.....

Dog. No.	Post op days	Liver	Gallbladder		Extrahepatic bile duct		Bile		
			Atrophy	Adherence	Thickness	Dilatation	Gallstone	Tubility	Foul-smelling
56	9	−	−	+	+	+	−	+	+
51	11	−	−	±	+	+	−	+	+
58	28	−	−	+	+	+	−	++	++
25	28	−	−	+	++	++	+	++	++
63	31	−	−	±	++	++	+	++	++
14	31	−	−	±	+	+	+	++	++
24	34	−	−	±	+	+	−	++	+
36	37	Abscess	−	+	++	++	−	+	+
27	40	−	−	+	++	++	+	++	++
43	59	−	−	+	+	+	+	++	++
47	64	−	−	+	++	++	+	++	++
60	65	−	−	±	++	++	−	+	+
39	70	−	−	±	+	+	−	+	+
55	73	−	−	±	+	+	+	+	++
62	75	−	−	−	+	+	+	++	+
59	98	−	−	++	+	+	+	±	+
61	148	−	−	−	+	+	+	+	+
54	183	−	−	−	+	+	+	±	+

2. Histological Pictures

The materials were examined in their hematexylineosin-stained specimens.

(1) The Gallbladder

A. In normal dogs

The gallbladder was found to have a mucosal epithelium composed of tall single-filed columnal cells, each with an ovoid chromatin-rich nucleus near its base. The mucosal layer proper was a sheet of cell-rich connective tissue supplied by blood vessels varying in diameter; the plain muscle was formed into a compact layer, the course of the muscle fibers being annular; the subserous tissue was coarse fibrous connective tissue. (Fig. 19)

B. In dogs which had undergone choledochojejunostomy

(a) On the 40th postoperative day: The folds on the inner coat of the gallbladder were irregular in width and fused two or three together, and one or two of them edematious; the epithelial cells of the mucosa were in a state of vacuolar degeneration; the coarse connective tissue extending from beneath the basal membrane to the muscle layer, particularly that lying beneath the basal membrane, was infiltrated mainly by polynuclear leukocytes, eosinophils and monocytes, and contained an increased number of reticular fibers and their mother cells, showing that it was proliferating on its may to recovery; in the muscle layer the muscle fibers were either diminished or torn, with connective tissue fibers newly formed among

them. (Fig. 20)

(b) On the 70th postoperative day: Small abscesses were present on the folds of the inner coat of the gallbladder; the mucosal epithelium looked like chorionic epithelium in some parts; the coarse connective tissue beneath the basal membrane was infiltrated by inflammatory cells; the muscle fibers in the muscle layer were irregularly arranged, cicatrized and were undergoing hyaline degeneration.

(c) On the 98th postoperative day: The mucosal epithelium was remarkably increased in number and thickness by proliferation, looking like the duodenal wall, and was atrophied and necrotized in parts; the coarse connective tissue beneath the basal membrane was infiltrated by inflammatory cell and presented a proliferation of lymph apparatuses; the muscle layer was in a state of hyaline degeneration. (Fig. 22)

(d) On the 183rd postoperative day: The inner coat was very irregular and the mucosal epithelium showed signs of vacuolar degeneration; the coarse connective tissue beneath the basal membrane had in it a remarkably increased number of lymph apparatuses, and the mucosal epithelium, strained under their pressure, was desquamated; the mucle layer was hyalized and cicatrized. (Fig. 23)

(2) The Extrahepatic Bile Duct

The extrahepatic bile duct was abscessed within its canal with bacterial colonies found in it; the mucosa epithelium was either increased by proliferation, or necrotized or deficient in parts. The coarse connective tissue beneath the basal membrane was infiltrated by inflammatory cells; in the muscle layer the muscle fibers were irregularly arranged and appeared hyalinoid. (Fig. 24)

(3) The Liver

The interstitial connective tissue was remarkably thickened; the lobules were atrophied and irregularly arranged, with many small abscesses produced in them; the liver cells were swollen, each vacuolized in its protoplasm; the GLISSON's capsule was diffusely infiltrated by inflammatory cells, with its blood vessels increased in number and with an increased number of reticulocytes occurring in it; the columnal epithelial cells of the biliary ducts were greatly dilated, and in some parts desquamated and deficient. (Fig. 25)

Incidentally, the dogs subjected to choledochojejunostomy were none of them found to be infested with any parasite.

CHAPTER VII. SUMMARY AND COMMENT

The value of total serum bilibubin, as determined after ligation of the common bile duct in normal dogs and in dogs submitted previously to choledochojejunostomy, was found to rise sooner after ligation in the latter than in the former group. In 2 of 6 cases in the latter group it rose above normal within the lst day after ligation and thereafter continued to rise noticeably. Especially in 2 of those 6 cases, it exceeded 1 mg/dl within 24 hours after ligation as it did in dogs in which the gallbladder was excised and the common bile duct ligated.

The fact that choledochojejunostomy produced no marked change in the secre-

tion of bile may be taken to imply that the operation resusts in course of time in a decline in or in the lose of the bile-concentrating function of the gallbladder.

The tonic contraction of the gallbladder, which is regarded as more important to the excretion of bile than any other movement of the organ, was traceable in normal dogs with the apparatus for measuring its internal pressure after intraduodenal infusion of the creamy mixture and subcutaneous injection of 1% pilocarpine hydrochloride, each a stimulant of the organ. But it had to be found out whether this procedure would succeed in tracing contraction of the gallbladder in dogs subjected to choledochojejunostomy with the common bile duct left open at its end. Contraction was practically untraceable by the same apparatus in dogs in which the common bile duct was connected to the jejunum by means of a rubber tube and was left open at its termination.

Then in other normal dogs, the common bile duct was cut through at its termination, a vinyl tube was inserted into the hepatic side of the duct, and the bile was led out of the body through this tube. In order to allow the bile to accumulate in the biliary duct to a certain amount, the vinyl tube was kept closed for a time before examination, for which the same apparatus was used. It was found on this occasion that tonic contraction of the gallbladder was provoked and more marked after subcutaneous injection of 1% pilocarpine hydrochloride than after intraduodenal insusion of the creamy mixture. Finally, the same apparatus was used for dogs subjected to choledochojejunostomy. The results showed that contraction of the gallbladder was traceable after subcutaneous injection of 1% pilocarpine hydrochloride, but not after intraduodenal infusion of the creamy mixture.

This fact is difficult to explain as long as the mechanism of the cholecystic movement remains unknown, but it appears that choledochojejunostomy leaves the gallbladder incapable of tonic contraction in response to such a physiological stimulation as is given by food entering the duodenum.

Choledochojejunostomy leaves the gallbladder with a foul-smelling mixture of bile and small gallstones. In its postoperative histological pictures, the gallbladder presented marked signs of inflammation; folds of its inner coat was unequal in width and edematous, and its columnal cells swollen and rendered dificient in parts; the coarse connective tissue extending from beneath the basal membrane to the muscle leyer was infiltrated by inflammatory cells, with an increased number of small lymph apparatuses in it; the muscle layer was hyalinized and degenerating with its muscle fibers arranged irregularly.

Such postoperative functional extinction of the gallbladder appeared to result mainly from the inflammation that developed in it postoperatively. It is conceivable, on the other hand, that as the operation ··· choledochojejunostomy ··· separates the common bile duct from the sphincter of Oddi, the gallbladder may not be required to cooperate with the sphincter and lose much of its working capacity.

Cholecystography by use of a contrast medium succeeded in obtaining a picture, of the gallbladder even if indistinct, in one of the dogs submitted to choledochojejunostomy. Because the flow of bile into the gallbladder is a prerequisite to the appearance of even an indistinct shadow, it follows from the above fact that some

of the bile was kept flowing into the gallbladder instead of all of it flowing into the duodenum despite the fact that the common bile duct was left open as a result of choledochojejunostomy. But this cannot be taken to be conclusive proof that the gallbladder retains its function as bile-reservoir after the ananstomosis.

Roux-Y anastomosis was used in this experimental choledochojejunostomy: the anastomosed junction of the common bile duct and the jejunum was kept a distance of some 30 cm apart from the entero-entero anastomosed part of the intestine in order to prevent any possible ascending infection reaching the gallbladder. The result was, however, that the gallbladder, the biliary duct, and the liver were all affected by a remarkable ascending infection. It is to be hoped that this technique of operation will be improved in this respect.

As has been described above, choledochojejunostomy is likely to deprive the gallbladder of its normal functions and leave it a sort of useless diverticulum and source of ascending infection. The presence of such a diverticular gallbladder may naturally be expected to further promote the spread of the inflammatory condition.

An early surgical treatment of cholecystitis has generally been recommended on the ground that the liver is frequently and quickly affected by the inflammation of the gallbladder. In fact, in this experiment, the liver was found to be inflammatory when the gallbladder was left unexcised. Thus it is only reasonable to conclude that the operation should be accompanied by the removal of the gallbladder to minimize the possibility of ascending infection.

CHAPTER VIII. CONCLUSION

1. It was noted that choledochojejunostomy reduces or eliminates sooner or later the bile-concentrating function and the motile function of the gallbladder, as examined in 18 dogs during a period of 9 to 183 days after the operation.

2. Macroscopically and histologically, the gallbladder was filled with infectious bile and its wall, the liver and the biliary duct all showed signs of inflammation after choledochojejunostomy.

3. Roux-Y anastomosis, namely separation of the anastomosed junction of the common bile duct some 30 cm apart from the entero-entero anastomosis site, failed to prevent an ascending biliary infection resulting from choledochojejunostomy.

4. The inflammation developing after choledochojejunostomy may more reasonably be minimized in severity if the operation is accompanied at the same time by the extirpation of the gallbladder because the operation leaves this organ a useless diverticulum filled with infectious bile, and its wall a site of inflammation.

I wish to thank Prof. Dr. Chisato Araki and Assist. Prof. Dr. Ichio Hosjo for their guidance throughout the period of this work.

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和文抄録

総胆管空腸吻合後 胆嚢の態度に関する実験的研究

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胆管腸吻合後，胆嚢は果して従来通りの機能を保持しているのか，又機能を減弱更には廃絶して萎縮するのか，更に憩室の如き状態にある為炎症を起こし易く反つて有害なのか，之等の点を解明する為に，実験動物として犬を用い，上行性胆道感染防止の為ルー氏Y字状吻合方法により，総胆管空腸吻合を施行し，一定時日後に胆嚢の各機能を検査すると共に，肝臓，肝外胆管及び胆嚢の肉眼的組織学的検索を行つた．

1. 濃縮能．

Mann & Bollman の実験を応用して，即ち総胆管を結紮して黄疸の出現状況より間接的にその機能を検したが，正常犬総胆管結紮例に比べ，総胆管空腸吻合犬では早朝より黄疸が現われる．又正常犬と総胆管空腸吻合犬との間に，胆汁の分泌量に著明な差を認めない事と併せ考えると，斯る総胆管空腸吻合犬では，胆嚢の濃縮能は一定時日後には減弱或いは消失するものと考える．

2. 運動能

胆嚢内圧描記装置を用いて，その機能，緊張性収縮運動の有無を検したが，斯る総胆管空腸吻合犬では，十二指腸内クリーム（卵黄＋バター）注入では収縮せず，1%塩酸ピロカルピン皮下注射では収縮した．

胆嚢の運動の発現機序が明確でない現在，この事を説明することは困難であるが，少くとも，総胆管空腸吻合犬の胆嚢の緊張性収縮運動は十二指腸内食物流入の如き生理的な刺戟では，最早や反応するに至らないものと解釈される．

3. 濃溜能．

ビリグラフインの静脈注射により胆嚢造影を検したが，斯る総胆管空腸吻合犬に於て，1例に不明瞭乍らも造影を認めた．この事は総胆管空腸吻合の如く，総胆管末端部が開放性になつていても，胆汁は一方的に十二指腸内にのみ流入せず，胆嚢内にも，或程度流入することを示している．

4. 肉眼的組織的所見として，胆嚢内は程度の差こそあれ，何れも感染性の胆汁で満たされ，且組織学的に胆嚢に主として慢性の炎症性変化を認めた．

斯る炎症性変化は，肝臓及び肝外胆管にも認めた．従つて，総胆管空腸吻合後は，胆嚢は，最早や正常の機能を営み得ず無用の憩室の如き状態にあり，他方，上行性胆道感染防止対策として，ルー氏Y字状吻合方法を用いたが，上行性胆道感染は避けられないことが明らかとなり，斯る総胆管空腸吻合の幾分でも術後の胆道の炎症を軽減する意味で，胆嚢の同時切除が合理的であると考える．

Fig. 16 Cholecystography in the normal dog

Fig. 17 Cholecystography in the dog on 164th day after choledochojejunostomy

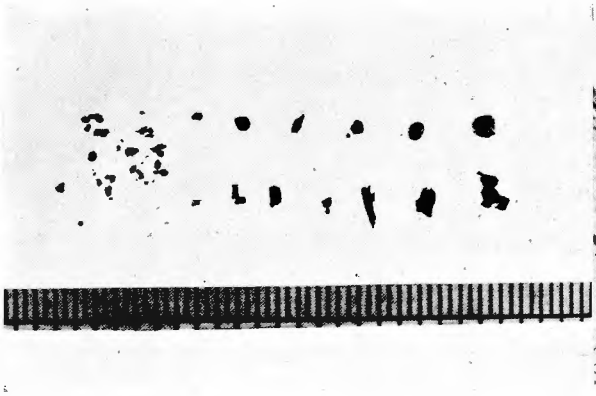

Fig. 18 Gallstone and food residuals in the gallbladder of the choledochojejunostomized dog

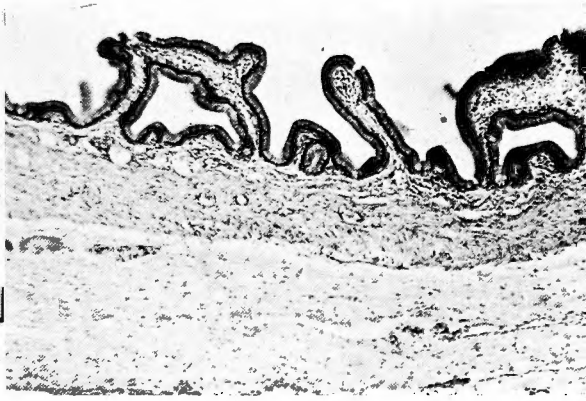

Fig. 19

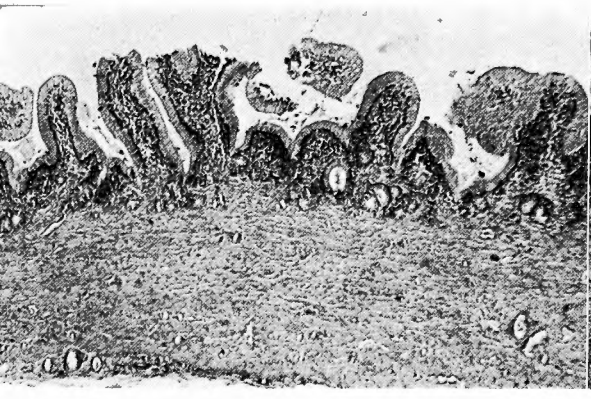

Fig. 20

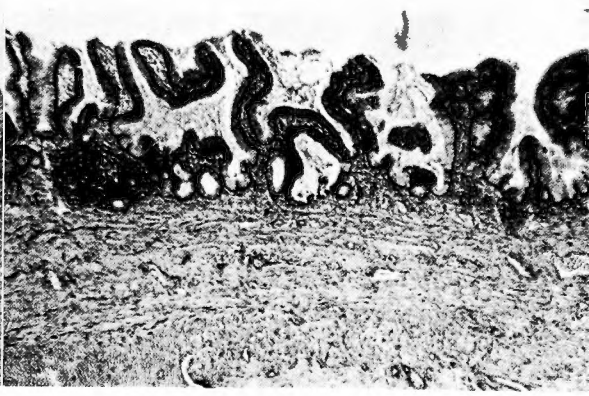

Fig. 21

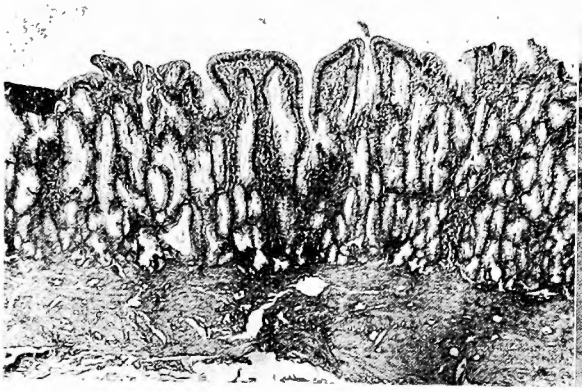

Fig. 22

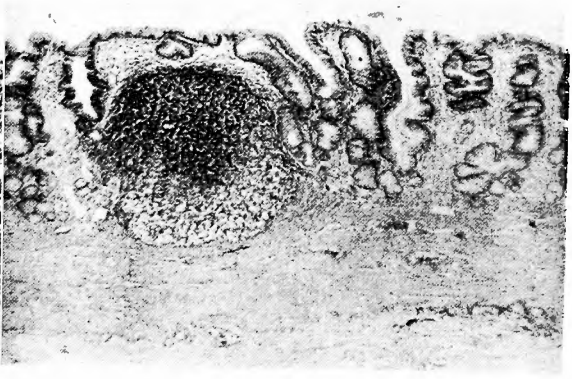

Fig. 23

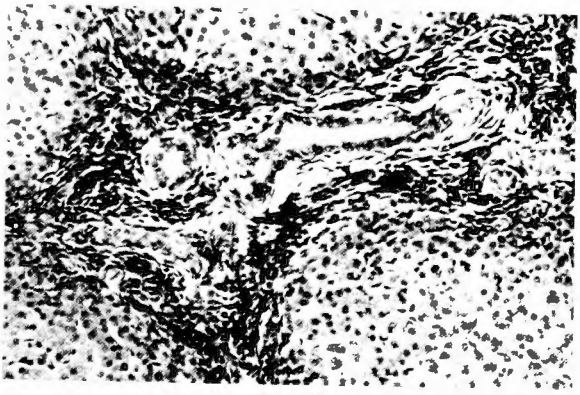

Fig. 25

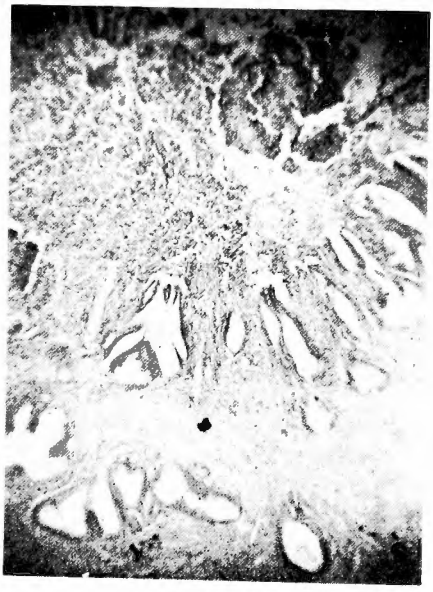

Fig. 24